SUMMARY

CHAPTER I

ASYMMETRIC SYNTHESIS OF OXIRANES - A REVIEW

Non-racemic oxiranes are important chiral synthons finding wider and wider applications in organic asymmetric synthesis. They have been used as key intermediates in the preparation of biologically active compounds such as leukotriene C-1, erythromycin, disparlure etc. This explains the great interest in the development of methods for the synthesis of optically pure oxiranes. The present review highlights certain important chemical methods available for the asymmetric synthesis of oxiranes.

The methodologies currently available for the chemical enantioselective synthesis of oxiranes have mostly centred around the epoxidation of alkenes. Two major routes are : 1. The Sharpless epoxidation applicable to allylic alcohols, and 2. Epoxidation with catalysts such as salen manganese complexes, certain porphyrins etc. mainly studied with unfunctionalized phenyl alkenes (styrenes).

CHAPTER II

ASYMMETRIC SYNTHESIS OF OXIRANES USING CHIRAL (1R,3S,4S,S_s)-(-)-S-METHYL-S-NEOMENTHYL-N-TOSYL SULFOXIMINE, 1a AND ITS EPIMER AT SULFUR (1R,3S,4S,R_s)-(+)-1b

One of the well entrenched methodologies for the synthesis of oxiranes is the methylene transfer (MT) reaction from dimethyl sulfoxonium methylide (Corey's Reagent) and related reagents to carbonyl compounds. Sulfoximines are another class of methylene transfer reagents used for the synthesis of oxiranes. As reported in the literature, the asymmetric synthesis of oxiranes using sulfoximines having stereogenic sulfur have not been very successful (ee, $<$ 40%). We felt that sulfoximines with suitable chiral ligands on stereogenic sulfur could be exploited for the synthesis of chiral oxiranes. Thus, we have prepared (1R,3S,4S,S_s)-(-)-S-Methyl-S-neomenthyl-N-tosyl sulfoximine, 1a and its epimer at sulfur (1R,3S,4S,R_s)-(+)-1b, possessing stereogenicity both on sulfur atom and on carbon atoms of the substituent groups. These reagents were used as MT reagents in the enantioselective synthesis of oxiranes from prochiral carbonyl compounds in fairly good enantiomeric excess (ee, 56-86%)[1]. The absolute configuration at chiral sulfur atom of sulfoximine 1b was established to be (R) and an intermediate sulfoxide to be (S) by single crystal X-ray structural analysis. Signs of optical rotation of oxiranes obtained using sulfoximine with (R) configuration at sulfur were opposite to those obtained using sulfoximines having (S) configuration at sulfur.

CHAPTER III

ASYMMETRIC SYNTHESIS OF OXIRANES USING CHIRAL $(1R,S_S)$-(-)-S-METHYL-S-EXO-2-BORNYL-N-TOSYL SULFOXIMINE, 2a AND ITS EPIMER AT SULFUR $(1R,R_S)$-(+)-2b

Assuming that replacement of the monocyclic neomenthyl group on sulfur in sulfoximine 1a and 1b (Chapter II) with the bicyclic *exo*-2-bornyl group should introduce more rigidity in the sulfoximine molecule and more steric crowding around the sulfur atom and that this should result in substantially higher enantioselectivity in MT reactions, we studied a new epimeric pair of sulfoximines viz. $(1R,S_S)$-(-)-2a and $(1R,R_S)$-(+)-2b. Sodium salts of these sulfoximines 2a and 2b on reaction with prochiral aldehydes and ketones gave chiral oxiranes with 19-68% enantiomeric excess[2]. It came as a surprise to us that changing the neomenthyl moiety on sulfur with a more rigid bicyclic chiral auxiliary such as *exo*-2-bornyl group resulted in lower ee in oxirane synthesized. The absolute configuration at sulfur of sulfoximine 2b was found to be (R) based on single crystal X-ray structural analysis.

CHAPTER IV

ASYMMETRIC SYNTHESIS OF OXIRANES USING (1R,3S,4S,1'S,R_S)-(+)-S-METHYL-S-NEOMENTHYL-N-(CAMPHOR-10-SULFONYL) SULFOXIMINE, 3b AND ITS EPIMER AT SULFUR (1R,3S,4S,1'S,S_S)-(+)-3a

In view of the results obtained so far, we decided to investigate whether a chiral auxiliary on nitrogen in addition to that on sulfur would enhance the asymmetric induction in these MT reactions. D-Camphor sulfonic acid appeared to us as the first choice as a chiral replacement for p-toluene sulfonic acid in the preparation of required sulfoximine. Accordingly, we prepared a new epimeric pair of sulfoximine 3a and 3b. Sodium salts of these sulfoximines on reaction with prochiral aldehydes and ketones gave oxiranes with 50-86% ee[2]. Replacement of the achiral tosyl group with a chiral camphor-10-sulfonyl group on nitrogen has no significant additive effect on the extent of asymmetric induction in MT reactions.

CHAPTER V

ASYMMETRIC CYCLOPROPANATION OF BENZYLIDENE ACETOPHENONE USING CHIRAL S-NEOMENTHYL AND S-EXO-2-BORNYL SULFOXIMINES

The cyclopropyl group is found as a basic structural element in a wide range of naturally occurring compounds in plants and microorganisms. There is a close correlation between the chirality of a molecule and its biological activities. The impact of the stereochemistry on activity requires stereoselective synthesis of three membered ring moieties. A brief introduction of the important available methods for the enantioselective synthesis of cyclopropanoids has been given in this chapter.

As reported in the literature, chiral sulfur ylides and carbanions derived from sulfoximines containing stereogenic sulfur have been used as asymmetric MT reagents across electrophilic alkenes like benzylidene acetophenone resulting into the formation of 1-benzoyl-2-phenyl cyclopropane with low to moderate asymmetric induction (7-49 %). We have utilized all the three epimeric pairs of sulfoximines (Chapter II to IV) in the cyclopropanation of benzylidene acetophenone to give 1-benzoyl-2-phenyl cyclopropane. Fairly good diastereomeric excess (de, 67.5-85%) was achieved in all the cases. This again proves that stereogenicity on substituent carbon atoms in addition to that on sulfur atom in a sulfoximine molecule enhances the enantioselectivity of MT reaction in cyclopropanation. An important observation is that all (S_S)-sulfoximines gave cyclopropane with (1S,2S) configuration in excess whereas all (R_S) sulfoximine gave (1R,2R) cyclopropane derivatives in excess.

REFERENCES

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